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Phase Transitions in Segmented Polyesterurethane–DMSO–Water Systems

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ABSTRACT: The phase separation processes occurring in polyurethane/DMSO/water mixtures were studied using DSC and cloud point measurements. It is demonstrated that liquid–liquid demixing occurs in ternary solutions of segmented polyesterurethanes at sufficiently high water concentrations. It is also shown that the hard segment can crystallize from solution when cooled to room temperature; while if the mixture is cooled to sufficiently low temperatures, DMSO partially freezes, which also induces crystallization of the soft segment. © 2005 Wiley Periodicals, Inc. J Polym Sci Part B: Polym Phys 43: 716–723, 2005
Keywords: polyurethanes; phase diagrams; phase separation; biomaterials; elastomers

INTRODUCTION

Polyurethanes are a group of polymers that are commonly investigated as basis material for scaffolds, which guide the body in the (re)generation of tissue.[1–3] The scaffolds are mostly in the form of foams with well-defined highly interconnected pores. The literature mentions several techniques for the formation of these porous structures. A few examples are freeze-drying, salt leaching, and rapid prototyping.[3–7] The major disadvantage of the generally used methods mentioned above is that it is difficult to combine a specific pore size with a tunable high interconnectivity and mechanical properties that should make the material suitable as meniscus scaffold. A method we described in literature does offer the combination of these properties, although this method has the complication that there are several phase transitions that all influence the spatial structure and mechanical properties of the foam.[8,9] Obviously, a clear insight in these transitions will enhance the knowledge of the foam formation and its properties. Unfortunately, research related to phase transitions of polyurethane solutions has been performed mainly on the basis of immersion precipitation and not on thermally induced phase separation (TIPS).[10–16] In the case of immersion precipitation, a polymer solution is immersed in a nonsolvent bath that will induce phase separation, possibly in combination with other transitions. With this method, the solvent composition changes with time while temperature is generally considered to be constant. In the TIPS method, the composition of the solution is kept constant while temperature is the variable.[8] Cooling of this solution will induce one or more phase transitions.

In this work, phase transitions will be presented for a polyurethane based on poly(ϵ-caprolactone) and 1,4-butanediisocyanate,[17] dissolved in DMSO–water mixtures. DMSO is used as solvent, and water is a nonsolvent for the polymer.

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DSC and visual observations are used to study the different phase transitions occurring in this system.

EXPERIMENTAL

Materials

Dimethylsulfoxide (DMSO, Acros) was distilled under reduced pressure from CaH_2.

The polyurethane used here is based on a soft segment of poly(ϵ-caprolactone) initiated on 1,4-butanediol (PCL) with a length of 1600g/mol. The hard segment (HS) is based on 1,4-butanediisocyanate and 1,4-butanediol and has a uniform length. The synthesis has been described earlier.[17] The polymer is abbreviated as PU1600. The number average molecular weight was 86.2kg/mol, with a polydispersity of 3.2.

GPC

Molecular weights (M_n and M_w) of the polyurethane were determined by GPC measurements using dimethylformamide with 0.01 M LiBr as eluents on a Waters 600 Powerline system, equipped with 2 mixed-C Plgel 5μ columns (Polymer Laboratories) at 70 °C. The data analysis was done using conventional calibration with polystyrene standards.

Differential Scanning Calorimetry

Solutions of the polymer in a solvent/nonsolvent mixture were prepared by first weighing a certain amount (between 10 and 30 mg) of polymer in large volume stainless steel DSC pans (Perkin–Elmer), and a specific amount of premixed solvent/nonsolvent was added with an adjustable micropipette.

A TA-Instruments DSC 2920 modulated DSC was used for studying the thermal transitions. Calibration of temperature and heat of fusion were performed using Indium. The slope of the curve was minimized. The samples were homogenized at 80 °C for 45 min, which was found not to change the molecular weight by possible degradation. Prior to the cooling scan, the sample was heated to 95 °C and kept at this temperature for 1 min. Subsequently, the samples were cooled to 20 °C or −10 °C and annealed at these temperatures for 45 and 5 min, respectively. The heating and cooling rates were 1 °C/min unless mentioned otherwise. In the case of a modulated scan, the average speed was 1 °C/min with a modulation of 0.5 °C per 60 s.

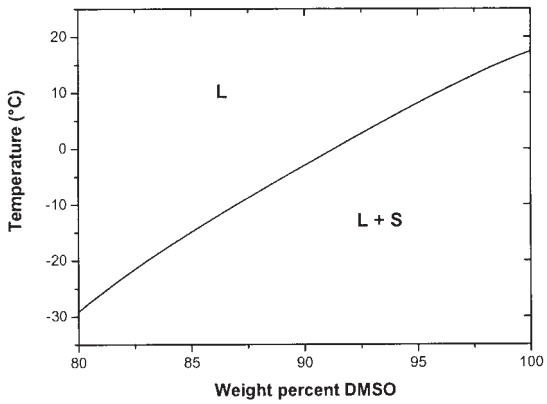

Figure 1. Part of the phase diagram for the DMSO–water system (plotted on a weight percent basis) with L as liquid DMSO–water phase and S as solid DMSO.[25]

Cloud Points

The polymer was dissolved at 80 °C with vigorous shaking for 20 min, after which air bubbles were removed by applying vacuum with a syringe. After a further 20 min of shaking, the mixture was cooled at a rate of 0.5 °C/min. The temperature of L–L phase separation was taken when the solution visually turned opaque.

RESULTS AND DISCUSSION

The scaffold preparation as described earlier is carried out using DMSO–water mixtures with compositions close to pure DMSO.[8] The relevant part of the phase diagram for these solvent mixtures was taken from literature and is reproduced in Figure 1. The behavior of the mixture upon cooling from 80°C can be derived from this diagram and consists only of freezing of pure DMSO in equilibrium with an increasing water concentration of the remaining DMSO–water mixture. We assume that this behavior is not largely influenced by the presence of the polymer.

When a polymer solution in DMSO–water mixtures is cooled, the phase behavior of the polymer in that solvent mixture is superimposed on the above-mentioned phase behavior of the solvent mixture. In principle, the following phenomena might occur during the cooling process: (1) L–L phase separation, (2) Hard segment crystalliza-

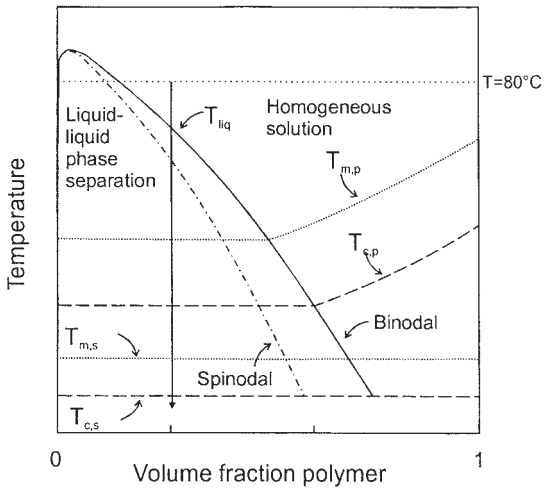

Figure 2. Schematic route through phase diagram upon cooling of a certain polymer concentration to below the freezing point of the solvent. T_{liq}: Liquid–liquid phase separation temperature, $T_{m,p}$: melting point of polymer, $T_{c,p}$: crystallization point of polymer, $T_{m,s}$: melting point of solvent, $T_{c,s}$: crystallization point of solvent. T = 80 °C represents the dissolution temperature of the polymer in the solvent mixture (which can be below the L–L phase separation temperature for certain concentrations).

tion, (3) Solvent crystallization, and (4) Soft segment crystallization.

All these transitions are schematically summarized in the theoretical phase diagram shown in Figure 2.

To determine what processes are actually occurring during the fabrication of the scaffolds and the consequences of this for the foam structure, we measured the phase behavior of PU1600 in different DMSO–water mixtures.

Liquid–Liquid Phase Separation

The first transition that is passed upon cooling the polymer solution is L–L phase separation: the polymer solution phase separates into a polymer rich and polymer lean phase. There are several methods that can be used to show this transition. Among others, DSC is a suitable method although a very high sensitivity is needed due to the small energy effects.[14,18–21] The influence of the amount of nonsolvent on the L–L phase separation temperature was tested with modulated DSC, but clear transitions were only found for polymer concentrations around 35%. Besides the low energy transition, the high viscosity of the solution might also impede the transition. Figure 3 shows the phase transitions on cooling of the polymer in DMSO with a varying amount of water. Clearly, an increase in water content leads to an increase in L–L phase separation temperature. In the case that no water was added, no transition was found at all.

The transitions were not visible in the heating scan, probably because of the long mixing time of the system. Longer annealing at 80 °C remixes the system and renders the transition visible again in the down scan.

The visual determination of cloud points confirmed the presence of the L–L phase separation for a 35% polymer concentration as was found with DSC, while the major influence of the nonsolvent water was also confirmed. In the absence of water, visually no phase separation was noted, while the addition of 6.75% water raised the phase separation temperature of a solution of 30% polymer to slightly below 80 °C, the temperature at which the polymers were dissolved. To prevent degradation of the polymer, the solutions were not heated above this temperature. This prevented the determination of the cloud point temperature of polymer concentrations below 30%, which were already phase separated at 80 °C.

Polymer solutions without water did not show a cloud point. At all temperatures the solutions were found to be homogeneous, which confirms the results derived from the DSC measurements.

When comparing Figures 3 and 4, a big difference in DSC and cloud point transition temperature can be found for the case of 35% polymer with 3.38% of water, which can be due to the

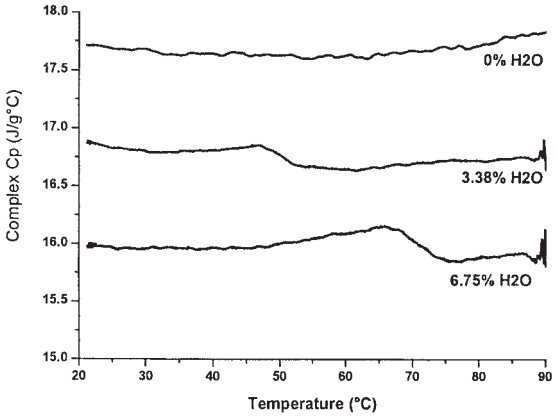

Figure 3. Influence of amount of H_2O on the L–L phase separation temperature of a 35% polymer solution as measured by DSC.

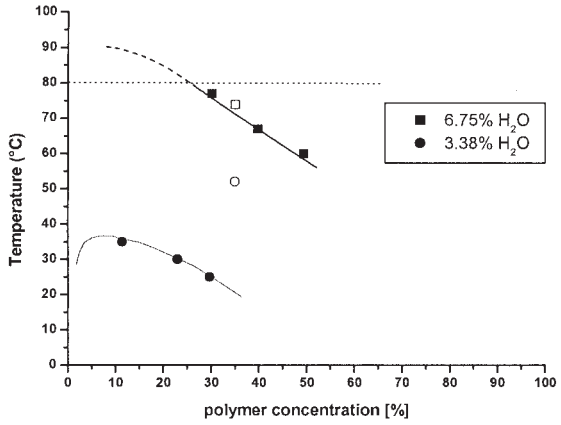

Figure 4. Influence of amount of H_2O on the cloud points visually determined and connected with an estimated cloud point curve. The open symbols are the values determined via DSC.

small difference in refractive index of the polymer rich and lean phase.[22] As a consequence, the cloud point is observed at a lower temperature than the liquid–liquid demixing temperature determined with DSC.

Both methods show that the small amount of nonsolvent has a major influence on the temperature of this transition.

Gelation

During the production of foams, it was noticed that the polymer solution showed a major increase in viscosity upon cooling. This suggests that a second phenomenon occurred in addition to the L–L phase separation. To elucidate this phenomenon, a DSC scan of a polymer solution of 35% of polymer in DMSO with 4.1% water was performed. First, the polymer was dissolved at 80 °C, after which the mixture was cooled with a scan speed of 1 °C/min to 20 °C modulated; subsequently, the mixture was heated to 80 °C with the same speed. Upon heating an exotherm slightly above 20 °C and an endotherm around 50 °C was found (Fig. 5). Since the DSC scan was performed modulated, we were able to distinguish reversible and nonreversible effects from each other. Reversible processes are generally transitions such as glass transition temperatures, while in general irreversible processes are crystallization and melting. In this case, both effects are only found in the nonreversible scan, which suggests that the effect was caused by crystallization in the case of the exotherm and melting in the case of the endotherm.

This crystallization and melting phenomenon is attributed to hard segment crystallization in solution instead of crystallization of a soft segment; a foam made in a similar way only shows a crystalline HS melting peak at 98.5 °C and no indications of a crystalline soft segment were found. The maximum theoretical melting point of poly(ϵ-caprolactone) is 70 °C.[23]

Since the HS crystallizes at temperatures below the L–L phase separation temperature, this phenomenon can occur in the polymer rich and/or the polymer lean phase. It is generally accepted that the polymer lean phase only contains a minor amount of polymer, which is negligible compared to the polymer present in the polymer rich phase. For this reason, we assume that the crystallizing polymer is the polymer present in the polymer rich phase.

Since gelation via crystallization is a nucleation controlled transition for which a certain degree of undercooling is needed, time is an important factor.[24] In the case of the thermogram without annealing at 20 °C, the HS started to crystallize during the heating scan (Fig. 6). For longer annealing times at 20 °C, it can be seen that more HS crystallizes. This suggests that the crystallization of HS is relatively slow. What also can be seen is that the melting point shows a slight decrease in temperature with increasing annealing time, from 51.3 to 49.0 °C, which is in agreement with the lower crystallization temperature.

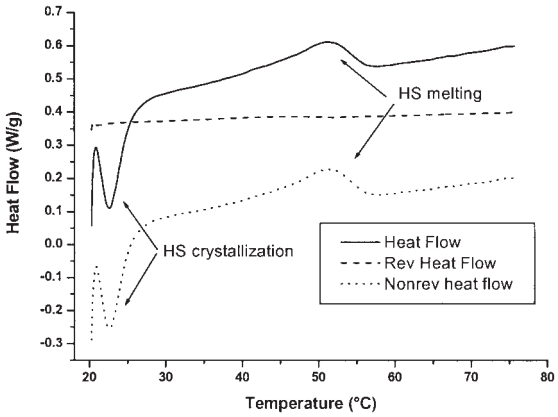

Figure 5. DSC heating curves (after cooling from 80 °C at 1 °C/min to 20 °C) without annealing at 20 °C of PU1600 in a 35% solution in DMSO containing 4.1% water.

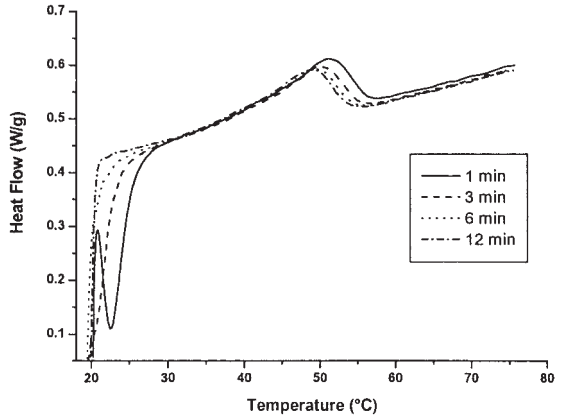

Figure 6. DSC heating curves after annealing at 20 °C for different times of PU1600 in a 35% solution in DMSO containing 4.1% water.

Figure 7 shows the influence of initial polymer concentrations on crystallization and melting after annealing for 45 min at 20 °C. A decrease in polymer concentration led to a major decrease in crystallization and accompanying melting temperature. For all except the three highest polymer concentrations, no exotherm was found in the cooling curve. Apparently no crystallization took place during cooling, but since a melting point was found in the heating scan, the HS must have crystallized during the 45 min of annealing at 20 °C.

Bulk polymer, without solvent, shows crystallization and melting temperatures of, respectively, 81 and 98 °C. The initial polymer concentrations of 10 and 20% with 6.75% of water were also mixed at 80 °C, which is, as can be seen in Figure 4, below the cloud point curve. They did not dissolve into a homogeneous solution, but in a polymer rich and poor phase. However, this did not lead to any deviations in the obtained melting points.

The solvent quality also influences the crystallization and melting temperature. Although for most samples the crystallization temperature is the same (during annealing at 20 °C), a clear difference is found in melting points at the same initial polymer concentrations (Fig. 7). For 40% polymer in combination with 0% water in DMSO, a T_m of 36 °C was found, whereas a water content of 6.75% at the same polymer concentration increases the melting point about 12 °C. This change in melting point with a variation in solvent quality is due to the increase in the L–L phase separation temperature with an increasing amount of water and the change of solvent quality (χ-parameter).

As soon as the solution passes the L–L phase separation boundary, a polymer rich and a polymer lean phase are formed. More nonsolvent leads to a higher L–L phase separation temperature, which, at constant demixing temperature, leads to an increase in the percentage of the polymer lean phase, which is accompanied by an increase in polymer concentration of the polymer rich phase, the phase where the HS crystallizes. In most cases, the hard segment crystallization temperature was constant, 20 °C. (This is schematically represented in Fig. 8. With an increase in demixing temperature, at constant temperature, the polymer rich concentration changes from A to B.) This higher polymer concentration will, in its turn, lead to a decrease in melting point depression and thus to a higher melting point.

Especially for the highest water concentration, one would expect an initial polymer concentration range in which the melting point remains constant. Below the L–L demixing temperature, the polymer concentration in the rich phase is constant and would thus give a constant melting point, which is not found, however. The deviation is most likely due to deviations from the assumption that the DMSO/water ratio is the same in the polymer rich and poor phase due to a difference in the interaction between polymer–DMSO and polymer–water, which has been seen for comparable systems.[12,13]

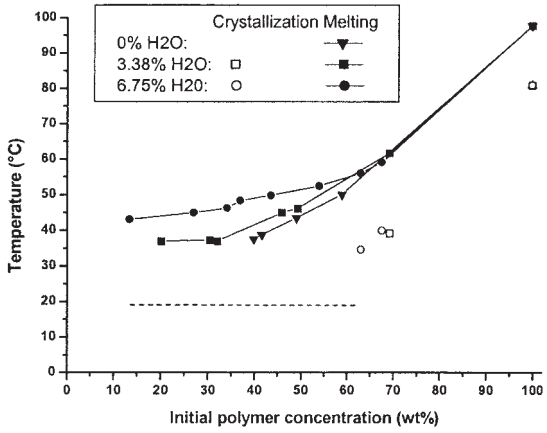

Figure 7. Crystallization and melting temperatures of PU1600 dissolved in DMSO with varying water concentrations as a function of the initial polymer concentration. Measured by cooling from 80 °C at 1 °C/min, 45 min annealing at 20 °C before heating at 1 °C/min.

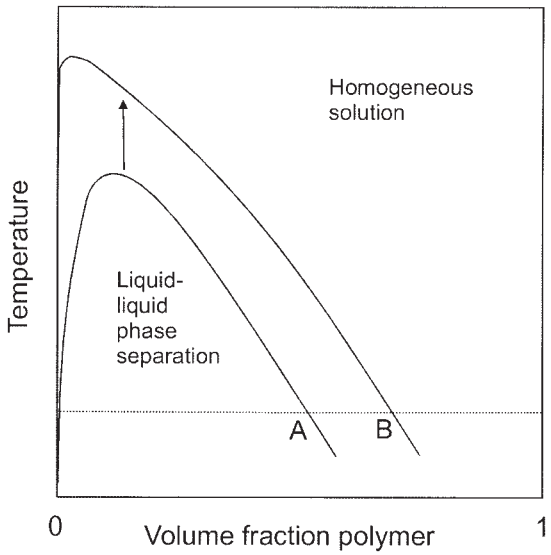

Figure 8. Schematic representation of the influence of the increase in L–L phase separation temperature on the polymer concentration of the polymer rich phase.

The amount of nonsolvent used also influences the lowest melting temperatures found under these circumstances. In the absence of nonsolvent, no melting point was found for polymer concentrations below 40%, while in the case of 3.38% or 6.75% water, melting points were found at polymer concentrations as low as 20 and 13%, respectively. This does not mean that HS cannot crystallize with lower polymer concentrations after longer periods of annealing. Even for concentrations of only a few percent of polymer, it was visually noted that opaque spheres were formed after several hours due to L–L phase separation with nucleation of the polymer rich phase, after which the HS in the polymer rich phase crystallized causing the opaqueness of the sphere.

Solvent Crystallization

If after gelation the solution is cooled to −10 °C, part of the DMSO will crystallize and induce further phase separation. The crystallization of DMSO in the polymer lean phase will not have a noticeable effect on the polymer since there is hardly any polymer present in this phase; but in the polymer rich phase, freezing of DMSO will initiate further phase separation. The polymer rich phase will form two phases; one phase contains only frozen DMSO, while the other phase contains gelled/precipitated polymer and solvent containing an increased amount of water. A schematic overview of the transitions is given in Figure 2.

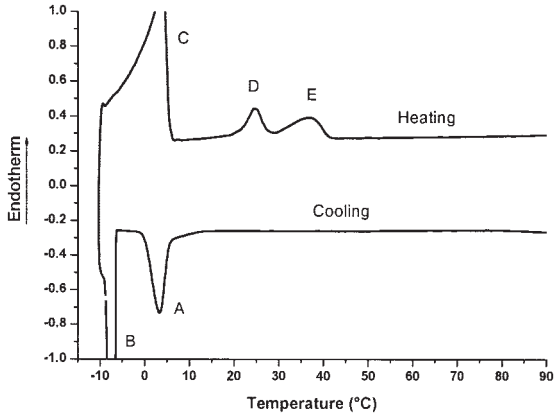

Figure 9. 35% PU1600 solution in DMSO containing 5.7% water. Before the heating scan, the sample was kept at −10 °C for 5 min. A: crystallization hard segment. B: Crystallization solvent and hard segment. C: Melting solvent. D: Melting soft segment. E: Melting hard segment that crystallized at A.

This extra transition will give a more complicated DSC thermogram. Figure 9 shows a complete heating and cooling curve of a 35% PU1600 solution in DMSO with 5.7% water. Upon cooling the HS crystallizes around 4 °C (peak A) and at −6 °C (peak B) the DMSO starts to crystallize. In the heating curve one can see that the solvent melts slightly above 0 °C (peak C), while two

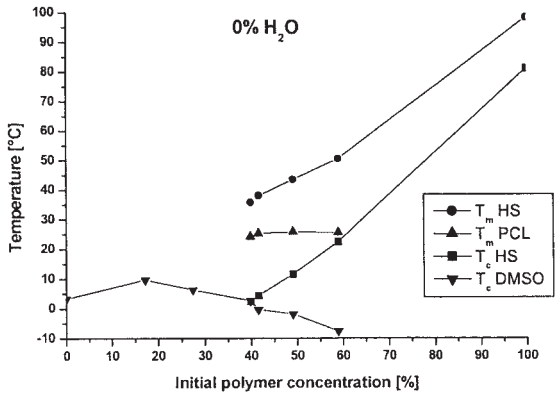

Figure 10. Crystallization and melting points as a function of polymer concentration in DMSO in absence of water. Measured by cooling to and 5 min annealing at −10 °C before the heating scan. T_c represents the crystallization temperature of the hard segment, T_m HS and T_m PCL represent the melting points of the hard and soft segment, and T_c DMSO represents the crystallization temperature of DMSO.

melting peaks (Peaks D and E) are found. In contrast, cooling to 20 °C only showed one melting peak in the heating curve. Earlier ATR-FT-IR measurements at different temperatures of foams made via this method showed that this extra melting peak originates from the crystalline soft segment, PCL, and not from the crystalline hard segment.[8]

To investigate the influence of the initial polymer concentration and the amount of water used, several DSC scans were made with different initial polymer and water concentrations (Fig. 10–12).

Compared to cooling to 20 °C, the first melting points (T_{m1}) are the same; these are caused by HS that crystallized at T_c. The extra transition here is the crystallization of the solvent at values between +5 and −10 °C. As mentioned before, the crystallization of DMSO causes additional phase separation of the hard segment and also the PCL was able to crystallize.

With a polymer concentration below 40% and without water, no HS T_m is found even though the solvent crystallized. This suggests that during freezing of the solvent, the hard segment did not get the opportunity to crystallize. As soon as some nonsolvent was added, all the samples measured showed some degree of crystallization of the HS.

CONCLUSIONS

The polyurethane synthesized as described in earlier work shows several thermal transitions upon heating or cooling when dissolved in a mixture of DMSO and water.

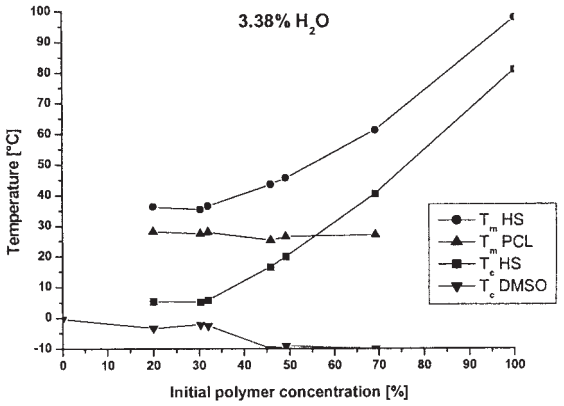

Figure 11. Crystallization and melting points as a function of polymer concentration in DMSO with 3.38% water. Conditions as in Figure 10.

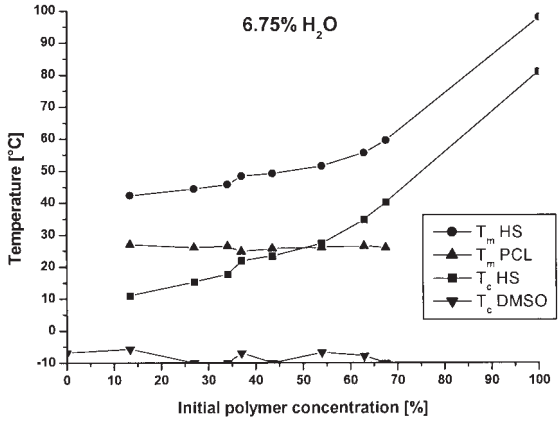

Figure 12. Crystallization and melting points as a function of polymer concentration in DMSO with 6.75% water. Conditions as in Figure 10.

Varying the amount of water that is used as nonsolvent changes the quality of the solvent. This makes it possible to dramatically change the liquid–liquid phase separation temperature by changing the solvent quality. With an increasing amount of water, the temperature at which liquid–liquid phase separation occurs can be increased. Moreover, at lower temperatures, the hard segment of the polyurethane crystallizes, depending on the initial polymer and water concentration.

When the polymer solution is cooled further, DMSO crystallizes. The crystallization of DMSO will change the quality of the solvent and will, in its turn, induce crystallization of PCL, although it seems that some hard segment has to be crystalline before PCL crystallizes.

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